August 10, 1999

Dockets Management Branch (HFA-305)
Food and Drug Administration
Room 1-23
12420 Parklawn Drive
Rockville, MD 20857

Re: **FDA Proposed Rule published April 29, 1998**

Dear Sir or Madam:

These comments are submitted by Roche Vitamins Inc. (Roche) to the Food and Drug Administration (FDA) pursuant to the Federal Register publication of April 29, 1998 relating to the FDA's proposed rule (63 Federal Register 23624).

Roche is a leading manufacturer and distributor of bulk vitamins, nutrients and other ingredients to food and dietary supplement manufacturers. Our comments are reflective of our support to provide valuable educational information about dietary supplements (including vitamins and minerals) to consumers which will empower them to develop and maintain healthy diets. As a result, health care costs will be reduced throughout the United States.

Although Roche would like to commend the FDA for certain aspects of this proposed rule, we believe that certain portions of this proposed rule exceed the authority of the FDA while other portions will stymie the dissemination of valuable health information to consumers (including new scientific knowledge and developments). We believe that these regulations, unless significantly modified, may lead to protracted, costly litigation. Roche urges the FDA to substantially revise the proposed rule to fulfill the spirit and intent of the Dietary Supplement Health and Education Act of 1994 (DSHEA), which clearly intended extensive educational information about dietary supplements to be disseminated to the American public. The proposed rule tends to confuse, rather than clarify, how, when and where structure/function claims may be used. The fact that so few of the claims submitted to the FDA to date have received comment letters proves that the industry (both supplements and foods) have an excellent understanding as to how DSHEA should be applied. Thus, our comments are as follows:

At the time of the passage of DSHEA, Congress stated a number of specific findings designed to elucidate the purposes of DSHEA. The theme of these findings was that there was a clear need to educate consumers about the health benefits of dietary supplements in order to improve the health status of United States citizens which would reduce health care costs in the United States. Thus, Congress found that:

- Improving the health status of United States citizens ranks at the top of the national priorities of the Federal Government;
- There is a link between the ingestion of certain nutrients or dietary supplements and the prevention of chronic disease such as cancer, heart disease and osteoporosis;
- Preventive health measures, including education, good nutrition, and appropriate use of safe nutritional supplements will limit the incidence of chronic diseases and reduce long-term health care expenditures;
- There is a growing need for emphasis on the dissemination of information linking nutrition and long-term health;
- Consumers should be empowered to make choices about preventive health care programs based on data from scientific studies of health benefits related to particular dietary supplements;
- Although the Federal Government should take swift action against products that are unsafe or adulterated, the Federal Government should not take any actions to impose unreasonable regulatory barriers limiting or slowing the flow of safe products and accurate information to consumers;
- Dietary supplements are safe within a broad range of intake, and safety problems are relatively rare; and
- Action that protects the rights of access of consumers to safe dietary supplements is necessary to promote wellness.

21 U.S.C. § 321, note, Pub. Law 103-417, §2. These findings make it clear that in enacting DSHEA, Congress intended for consumers to be “empowered” to make vital choices affecting their health care through the free flow of accurate information concerning dietary supplements. Unfortunately, certain sections of the proposed rule are contrary to this intent and do not provide clarity to industry. FDA has ignored the spirit of DSHEA, as intended by Congress, to educate and inform consumers so that consumers can make an informed judgment. The industry does not need further restrictions as FDA has proposed. FDA already has sufficient enforcement measures at its disposal which it is effectively using.

Roche believes it would be inappropriate for FDA to issue any regulation which would restrict the scope of statements of nutritional support related to a nutrient content claims and claims pertaining to a classical nutrient related disease. Claims such as “calcium builds strong bones” are permissible and should continue to be permitted. This fact should be clarified.

Roche also believes the FDA should clarify that the proposed rule applies for claims on both food and dietary supplement products.

Roche believes that the FDA’s proposed rule does not accurately reflect the Congressional intent in permitting statements of nutritional support, including structure/function statements, for dietary supplements. Under the plain language of DSHEA, a statement is permitted for dietary supplement if it:

- describes the role of a nutrient or dietary ingredient intended to affect the structure or function in humans, or
- characterizes the documented mechanism by which a nutrient or dietary ingredient acts to maintain such structure or function, or
- describes general well-being from consumption of a nutrient or dietary supplement.

Congress expressed only one caveat to the foregoing -- that a statement of nutritional support “may not claim to diagnose, mitigate, treat, cure, or prevent a specific disease or class of diseases.” The reference to a “specific” disease or class of diseases calls for a narrow definition of disease rather than the extremely broad spectrum of “deviations, signs and symptoms” FDA proposes to view as “diseases.” The term “specific disease” should refer to specific conditions such as gastric cancer, lung cancer, or prostate cancer, and the term “class of diseases” should refer groups of specific diseases such as “cancers.” It is inappropriate for FDA to attempt to extend these terms to include a variety of conditions and symptoms which are not strictly “diseases”, medically or legally. The statutory caveat does not mention “symptoms”, “signs”, “interruptions”, “deviations” or “impairments” of the normal structure or function. Thus, there is no reason for any of the new definitions proposed by the FDA. It is very clear what Congress intended and the current statutory definition in DSHEA is consistent with the NLEA.

THE DEFINITION OF DISEASE

The FDA proposes to establish new definitions of the term “disease” for purposes of determining whether structure/function statements are disease claims, and to modify the health claims definition of disease to be consistent with this new definition. Below is a comparison of the new and old definitions of disease in 101.14 (general requirements for health claims) and the new FDA proposal to establish a new definition of “disease” in 101.93(g) (certain types of statements for dietary supplements).

NEW (FOR HEALTH CLAIMS)	OLD (FOR HEALTH CLAIMS)	NEW (FOR DIETARY SUPPLEMENTS)
Disease or health-related condition means any deviation from, impairment of, or interruption of the normal structure or function of any part, organ, or system (or combination thereof) of the body that is manifested by a characteristic set of one or more signs or symptoms (including laboratory or clinical measurements that are characteristic of a disease), or a state of health leading to such deviation, impairment, or interruption; except that diseases resulting from essential nutrient deficiencies (e.g., scurvy, pellagra) are not included in this definition (claims pertaining to such diseases are thereby not subject to this section of 101.70).	***Disease or health-related condition*** means damage to an organ, part, structure, or system of the body such that it does not function properly (e.g., cardiovascular disease), or a state of health leading to such dysfunctioning (e.g. hypertension); except that diseases resulting from essential nutrient deficiencies (e.g., scurvy, pellagra) are not included in this definition...”	***A disease is*** any deviation from, impairment of, or interruption of the normal structure or function of any part, organ, or system (or combination thereof) of the body that is manifested by a characteristic set of one or more signs or symptoms, including laboratory or clinical measurements that are characteristic of a disease.

In the preamble of the proposed rule, the FDA states that the current definition of disease is too narrow in some respects and that the term “damage” can be interpreted as limiting the definition to serious or long-term diseases, or excluding certain conditions such as headaches. The FDA further points out that the health claims definition is broader than the dietary supplement definition of disease for purposes of structure/function statements because the health claims definition includes “health-related conditions as well as actual diseases.“ It is further stated that the proposed definition of disease is based on “standard medical and legal definitions of the term“ (but the FDA cites four different references).

The FDA further states that the proposed rule only applies to structure/function claims and disease claims and that “the proposed rule is not intended to apply to products other than dietary supplements for human consumption nor to interpret other provisions of the act.” Clearly, a “disease” is a “disease” and the definition of a disease should be the same for any category of products whether the product is a prescription drug, OTC drug, a dietary supplement, or a food.

Roche is adamantly opposed to any new or expanded disease definition. The FDA should not initiate any discussion of structure/function claims by deliberately expanding the definition of “disease.” Roche believes the proposed expansion of the disease definition exceeds the statutory definition mandated by Congress and constitutes legislation which the FDA has no authority to promulgate. It is abundantly clear that industry without any guidance by the FDA to date has been substantially complying with DSHEA. These proposed new definitions will only create a new wave of confusion leading to expensive litigation. This expanded definition will complicate rather than clarify the provisions of DSHEA.

Roche further suggests no definition of disease or health related condition should incorporate the phrase “structure or function.” It seems that the purpose for the expanded definition is to include more conditions requiring FDA pre-authorization, to exclude permissible statements of nutritional support and structure/function claims, to stop the dissemination of valuable educational information to the consumer and to confuse industry and consumers.

In lieu of the proposed definition, FDA could furnish guidance to the industry by giving examples of permissible claims which have already been furnished to the FDA and meet the current statutory provisions of DSHEA. We believe that the FDA’s guidance should state that disease does not include natural states or processes. FDA could clarify that “a natural state or process is a life change or physiologic manifestation expected in the normal course of life progression that is not a disease such as .....” Under this clarification, headaches, pregnancy, cessation of lactation, menopause, among other natural states or processes, would not in and of themselves constitute a disease or a symptom of a disease.

In fact, FDA states in the preamble that certain natural states, such as pregnancy, aging, headaches, or the menstrual cycle, are not a "disease." We agree with this statement. However, the FDA goes on further to state that these natural states are sometimes associated with abnormalities that are characterized by a specific set of signs or symptoms. We disagree. We do not believe headaches are a disease and we further believe almost all consumers would agree that headaches are not a disease. The proposed clarification is consistent with the FDA's authority, the findings of Congress, consumers knowledge of what a disease is, and would allow the dissemination of valuable information to the public. For these reasons, we further believe any reference to "natural state" under the proposed rule for disease claims should be deleted.

Roche further suggests that FDA use the following guidelines as the basis of determining whether a reference to a particular claim constitutes a disease claim:

a. The words, diagnose, prevent, treat, cure, mitigate (or other grammatical forms of these verbs) should not be used in a statement of nutritional support (i.e., a structure/function claim), since statements permitted under 403(r)(6) of the Act "may not claim to diagnose, mitigate, treat, cure, or prevent a specific disease or class of diseases;"

b. The words, stimulate, maintain, support, raise, lower, reduce, increase, decrease, improve, regulate, and promote -- or other words of this nature or other grammatical forms of these verbs -- may be used in a structure/function claim to distinguish the claim from a disease claim;

c. Clinical endpoints that are recognizable to health professionals or consumers as being related to a disease may be used in a structure/function claim, provided that the claim is constructed in accordance with points a. and b. above.

Rather than taking the negative approach and stating in the proposed rule what a company cannot state by expanding the definition of the word disease, FDA should clearly state what a company may state and what is not permissible. Although we commend the FDA for providing examples, overall these examples are ambiguous and confusing ("lowers cholesterol" vs. "maintains a healthy cholesterol level"). These examples do not provide clear, plain language guidance to either the consumer or industry.

Vitamin and mineral products aid, support and maintain normal body processes, structures and functions which promote good health, wellness and prevent illness. Vitamins and minerals are essential to provide good health to the American public. Scientific studies, journals, textbooks have documented the benefits of vitamins and minerals in preventing numerous diseases and maintaining good health. The Congressional findings of DSHEA confirm this fact when it was stated that: "There is a link between the ingestion of certain nutrients or dietary supplements and the prevention of chronic disease such as cancer, heart disease and osteoporosis."

It seems that the FDA's current proposed rule is an attempt to "regulate" rather than guide and/or clarify DSHEA, and that the FDA has found itself "splitting hairs" and engaging in "circular semantics."

It is very clear from the FDA's own research that consumers cannot differentiate between structure/function and approved health claims on labels. The FDA's proposed rule will not help in this regard and will hinder consumer understanding of label content.

The FDA should not establish markers as a moving target under which a particular statement of nutritional support may be acceptable one year and may be classified as a "disease claim" the following year, based on an evolving consensus that the symptom is a surrogate marker for a disease. Such an outcome would be ludicrous and would be contrary to the entire intent of DSHEA.

The FDA should not construct barriers to the use of structure/function claims through an undue focus on what the FDA believes is the ultimate implications of statements as long as the claims and information is truthful and not misleading.

The fact that an educated consumer may make the connection between a structure/function statement and disease prevention should not be a hindrance or impediment to informing and educating the general public. We believe this point illustrates and captures the true Congressional intent and spirit of DSHEA.

There will always be an extension of a structure/ function effect to a disease. Therefore, extensions of the structure/function effect must be rejected as a basis for distinguishing between a disease claim and a structure/function statement.

One of the important benefits of vitamin/mineral supplements and fortification is to counterbalance drug/nutrient interaction or depletion in the body caused by the use of a drug or food. There are many prescription drugs which deplete the body of nutrients. Likewise, olestra is a component of food which depletes the body of certain nutrients. Would statements regarding the benefit of vitamins in

these cases be permitted? Roche does not believe so based upon the provisions of the proposed rule.

FDA's clarification of the term "disease" should not be constructed or construed to restrict or otherwise alter the provisions of DSHEA relating to already permissible structure/function claims for dietary supplements.

Roche cannot agree that normal alcohol intoxication (such having a couple of drinks or a hangover) or constipation is a disease. We have also previously commented upon what we believe the terms class of disease or disease means.

Roche further disagrees with the next classification of diseases. "Improves urine flow in men over 50 years old," "relieves headaches" and other examples provided are claims which should be permitted as consumers readily understand this terminology and they are not diseases. Even under the examples given under in another section by the FDA, the statement "for men over 50 years old" is permitted. FDA has acknowledged that: "This can be a difficult distinction conceptually, especially if the only reason for maintaining normal function is to prevent a specific diseases associated with abnormal function." If this is the case, why does the FDA then try to proceed? There will always be an extension of a structure/function effect to a disease. The FDA is now attempting to prohibit claims which are already clearly permitted by the statutory provisions of DSHEA. The FDA is creating a muddy standard which will lead to confusion and expensive litigation.

Roche also believes that the FDA should not apply the concept of disease to the normal consequences of aging and to the normal symptoms of natural cycles. Hot flashes, premenstrual syndrome and sexual function are not diseases and cannot be compared to Alzheimer's disease. We have also previously commented upon natural states and refer you to our prior comments.

Roche commends the FDA for recognizing that product names such as "CardioHealth" and "Heart Tabs" are permissible, but the language contained in the proposed rule is unclear as the words "has an effect on" could be interpreted by the FDA to mean almost anything. Many products currently in the marketplace similarly refer to colds or other diseases. Is the FDA now stating that these products which have been in the marketplace for years are not permitted because they are making a disease claim? The industry clearly believes these products are allowed by DSHEA and should not be treated as disease claims. The FDA should declare that the names of these products are permissible or provide further guidance as the statutory language is overbroad.

With respect to referring to an ingredient, if an ingredient may be truthfully mentioned in the existence of a compound, it should not be considered equivalent to making a disease claim as it is "truthful and not misleading." Many

different vitamins and minerals are contained in multivitamins, dietary supplements and food. Why could this fact not be mentioned?

Companies have been using statements, or are using product names, incorporating the word “cold” for years. The FDA has recently sent “courtesy letters” to a number of companies objecting to statements relating to a product’s effect in supporting the immune system during “cold and flu season.” In many cases, the statements had been made since the passage of DSHEA, and companies have assumed that FDA’s previous silence suggested that this type of statement was acceptable. Clearly, why is this statement not permissible? The object is to provide clear, truthful, nonmisleading, plain language to the consumer to empower them to make choices and these statement should be permitted. Trying to draw a bright line around semantics or commonly understood terms in order to expand the definition of a drug should not be done.

For the FDA to forbid any citation in labeling of articles or books whose titles include reference to disease goes too far. Labeling often includes highly informative and balanced, peer-reviewed scientific information which is valuable to the consumer. Clearly, articles or references from textbooks, JAMA, the New England Journal of Medicine or other bona fide textbooks and peer-reviewed scientific journals should be permitted, notwithstanding the fact that the article may mention a specific disease. It would be a restriction of freedom of speech to prevent citation in labeling of relevant articles and information whose titles happen to include reference to a disease. Important scientific information regarding vitamins and minerals should be allowed to disseminated to the public.

The FDA should not be making decisions for the consumer, but should allow the free dissemination of truthful and not misleading information to the public who will make the choice whether or not to use the dietary supplement. Consumers should be informed promptly and effectively of important new peer-reviewed, scientific developments and knowledge. This is being done every day on television, newspapers and other similar forums. In an effort to assist the industry and the consumer, the FDA should clearly state how scientific studies and emerging science may be cited as no guidance is given in the proposed rule. This is extremely valuable information which should be communicated to the American public in order for them to maintain good health.

Roche agrees with the FDA that an approved health claim is the final authoritative standard connecting the intake of a dietary supplement and/or food and the prevention of a medically recognized disease. However, Roche also believes that consumers should be informed and educated regarding the potential medical benefits, i.e., evolving science, of a health practice (e.g., women taking folic acid to prevent birth defects) from peer-reviewed scientific articles. For years information regarding the intake of folic acid and its correlation to birth defects was not allowed to be disseminated to women and the

general public as there was no health claim for folic acid, notwithstanding the fact that there was significant, peer-reviewed scientific articles that certain types of birth defects could be avoided. Clearly, consumers should have been informed of this valuable scientific information and given the choice of determining whether or not to take supplements and food containing folic acid to prevent birth defects in their unborn children. Now, fortification is required. Why should it have been so many years until consumers were given this choice? Is the FDA stating that information of this type from a scientific study could not be disseminated because it mentioned a disease? Roche believes this type of information should have been made available to the American public notwithstanding that an article or book mentions a disease.

There is also ample evidence that Congress recognized the evolution of nutritional science and the ever-increasing correlation between diet and chronic disease. Congressional enactment of NLEA and DSHEA bear witness to that recognition and the Congressional findings set forth earlier in this letter bear witness to this fact. It is no small coincidence that the word “Education” appears in the title of both of these important pieces of legislation.

Congress would not have established (under DSHEA) an Office of Dietary Supplements within the National Institute of Health to conduct and coordinate scientific research to determine the use of dietary supplements to “limit or reduce the risk of diseases such as heart disease, cancer, birth defects, osteoporosis, cataracts, or prostatism” and not intended for this new information to be communicated to consumers.

The Food Nutrition Board stated in The Institute of Medicine document in 1994 entitled “How Should the Recommended Dietary Allowances Be Revised?” that “as indicated by this review, nutrition science, similar to all scientific endeavors, is rapidly changing and evolving. Nutrition scientists and practitioners continue to learn more with each passing day about nutrition and its effect on health.” The proposed rule, if adopted, is directly opposite the Food Nutrition Board’s compelling evidence that good nutrition reduces the risk of chronic disease such as cancer, heart disease and osteoporosis as the proposed rule will not allow dissemination of this information.

Certainly, the FDA should take this scientific progress and evolution into full account when trying to guide industry on how they can best inform and educate consumers (via labeling) on emerging science. Roche believes that the FDA should encourage more rather than less education, given today’s knowledgeable consumer.

Roche also believes that the FDA has ignored the fact that most Americans do not eat a “balanced” diet and do not eat the daily recommended servings set forth on the food pyramid. Thus, in order to maintain a healthy lifestyle,

supplements and fortified foods are necessary in most American diets in order to avoid nutritional deficiencies of vitamins and minerals which can lead to disease, premature aging and other physical ailments. If the proposed rule is adopted, information of this type, as well as the correlation between diet and disease, could not be furnished to consumers.

The uses of pictures and other means should be permitted. How can a consumer determine an unhealthy "electrocardiogram tracing?" Under the proposed rule "Hearttabs" are permitted, yet a company could not put an electrocardiogram on its product. Once again, clear guidance is not given. Roche also believes that pictures of a healthy heart, artery or organ should be permitted.

A company should also be able to identify classes of products or compounds which are present in a product as long as it is truth and not misleading. Vitamins and minerals are classes of products. Is the FDA stating that a company could not state that daily consumption of vitamins and minerals may prevent the onset of disease and other physical ailments? Obviously, this fact is well known, but would not be permissible under a literal reading of the proposed rule.

Companies should also be permitted to refer to the nature of a product as long as it is truthful and not misleading. Roche does agree with the FDA that there should not be a specific parallel between a branded drug and a dietary supplement.

Roche further believes that under the next two sections of the proposed rule, valid, scientific information regarding the role of vitamins and minerals in preventing disease and other conditions would not be permitted as the only exception provided by the FDA in the proposed rule is "other than a classical nutrient deficiency disease." One of the important benefits of vitamin/mineral supplements and fortification is to counterbalance any drug/nutrient interaction or depletion in the body caused by the use of a drug or food. Under the literal reading of these proposed rule, truthful and not misleading information regarding this role of vitamins and minerals would not be permissible as statements regarding a product maintaining good health would imply that its use will help you prevent a disease. Roche believes that such statements as "supports or maintains the body's resistance," "reduces the risk of" and "helps maintain good health" are permissible. The FDA should not issue any prohibition against general statements about health promotion and wellness. Roche further believes these statements are currently permissible under NLEA and DSHEA and should remain permissible.

The FDA uses overreaching language by proposing the following phrases in the proposed rule: "has an effect on a specific disease or class of diseases", "has an effect on a consequence of a natural state," "has an effect on disease through one or more of the following," "augments a particular therapy or drug action"

(vitamin E is taken by most heart patients as part of their therapy), “has a role in the body’s response to a disease or to a vector of disease” or “treats, prevents, or mitigates adverse events associated with a therapy for a disease and manifested by a characteristic set of signs or symptoms.” Vitamins and minerals are known to cure as well as prevent certain diseases and help to maintain good health. It seems clear that the proposed extremely broad, legal language was not drafted to provide guidance to the industry but for enforcement purposes. The FDA could arbitrarily use any of the foregoing unclear, overbroad regulatory language to disallow any claim, including but not limited to claims which are currently permissible under the NLEA and DSHEA. As such, whether or not this language is constitutional is highly questionable.

In addition to all of the above, the FDA then uses the new “catch-all”, all encompassing section which states that a statement will be viewed as a disease claim if it “otherwise suggests an effect on a disease or diseases.” As previously stated, this is unclear, overreaching and broad language by the FDA which would encompass any claim, including any current permissible structure/function claim.

The proposed rule does not provide clarity to industry and consumers, and as currently proposed, will allow the FDA to arbitrarily change its criteria from time to time to make any claim a drug claim and to chill the flow of valuable important health information to consumers about vitamins and minerals which will be to the detriment of the American public.

Roche would suggest that the FDA adopt the same standards as the FTC so that both agencies would be consistent in both interpretation and enforcement - that clear and simple standard being a “truthful and nonmisleading” standard, rather than creating a new unworkable, complex maze of regulations under which any claim, including any structure/function claim, may be interpreted by the FDA as a drug claim and enforced as such. Thus, there would be one consistent standard for both the FTC and FDA.

Congress clearly indicated in the “findings” that the intent of DSHEA was to increase health and education information to consumers about the health benefits of dietary supplements, specifically including the potential for decreasing the risk of disease and reducing health care costs, so that consumers would be empowered to make their own decisions. The proposed rule may lead to expensive, protracted litigation which is not in the best interest of the FDA, the industry or consumers.

The proposed rule is overreaching, both medically and legally; and does not promote the larger concept of promoting wellness and long-term health. It seems that the FDA is trying to create new barriers on the dietary supplement and food industries’ ability to communicate valuable information about dietary

supplements by, among other things, redefining the word “disease” and proposing the new provisions outlining disease claims. This is contrary to Congressional intent and findings, NLEA and DSHEA. The proposed rule, if enacted, will impose unreasonable regulatory barriers limiting or slowing the flow of safe products and accurate information to consumers. This is inconsistent with the Congressional intent and findings of DSHEA. Therefore, Roche strongly recommends that the FDA not issue the proposed rule as a final rule without significantly amending its language, focus and tenor from regulation and enforcement to guidance, especially in deleting any new disease definition.

Should Roche be able to assist the FDA in any way, please feel free to contact Mr. Bohm at (973)235-4295, Mr. Frank Girardi at (973)257-8325 or Dr. Vishwa Singh at (973)257-8347.

Respectfully submitted,

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